Characteristics and Risk Factors of Aspiration in Lateral Medullary Infarction

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Objective: To evaluate the characteristics of dysphagia and identify the risk factors of bolus aspiration in patients presenting with pure lateral medullary infarction (LMI).
Methods: Between January 2014 and January 2019, 51 post-stroke patients with LMI who underwent a videofluoroscopic swallowing study (VFSS) were enrolled retrospectively, and their medical records and brain magnetic resonance imaging results were reviewed. The VFSS results were evaluated to analyze the swallowing function using the penetration-aspiration scale, functional dysphagia scale, and imaging analysis software.
Results: Bolus aspiration was detected in 21 patients (41.2%). The common abnormal VFSS findings were residue in valleculae (74.5%), delayed triggering of pharyngeal swallow (72.5%), residue in pyriform sinuses (62.7%), delayed pharyngeal transit time (56.9%), reduced laryngeal elevation (51.0%), and coating of the pharyngeal wall (49.0%). The incidence of aspiration was significantly higher in the typical lesions (including the diagonal band-shaped lesions) and the large type lesions extending ventrally or dorsally, as compared to other lesion types ($P<0.05$). Logistic regression analyses revealed that the residue in pyriform sinuses is a significant independent risk factor of aspiration in the puree trial, and prolonged pharyngeal delay time (PDT) and residue in valleculae are significant risk factors in the thin liquid trial ($P<0.05$).
Conclusion: Considering all clinical factors, lesion locations, and swallowing processes, results of the current study indicate that residue in pyriform sinuses is an independent risk factor of aspiration in the swallowing puree technique, whereas prolonged PDT and residue in valleculae are independent risk factors of aspiration in the swallowing liquid technique. **(JKDS 2020;10:113-122)**

Keywords: Dysphagia, Aspiration, Lateral medullary infarction

INTRODUCTION

Dysphagia is one of the most common problems and an indicator of poor prognosis after stroke. It also increases the risks of aspiration pneumonia, dehydration, malnutrition, and mortality[1]. Lateral medullary infarction (LMI) especially evokes more severe and frequent dysphagia than other stroke lesions because central pattern generators (CPGs) for swallowing are known to exist in the lateral medullary

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region[2]. The incidence of dysphagia in patients with LMI has been reported to be approximately 57% to 69%[3,4], but dysphagia caused by LMI shows a wide distribution of severities.

Previous studies reported that delayed swallowing reflex[5], reduced pharyngeal contractions[6], upper esophageal sphincter (UES) opening failure[6-9], and disruption of the spatiotemporal pattern[10,11] were observed in patients with LMI. Some clinical-radiological correlation studies showed that dysphagia was more frequent in the rostrally located lesion in LMI[12,13]. Oshima et al.[7] reported that the presence of a passage pattern abnormality and greater vertical spread of the lesion can be useful predictors of severe dysphagia in LMI.

To ensure swallowing safety, it is essential for clinicians and researchers to identify patients at risk of bolus aspiration, such as clinical, neuroradiological findings and physiological impairments that most strongly influence the aspiration. This may help in planning for a proper intervention and improvement of rehabilitation outcomes. However, the risk factors of aspiration were still unclear in LMI. Most previous studies did not focus on bolus aspiration but clinical severity of dysphagia, and did not assess the entire swallowing functional process using functional dysphagia scale (FDS) and kinematic analysis of VFSS objectively in patients with LMI.

Therefore, this study aimed 1) to evaluate the characteristics of dysphagia and 2) identify risk factors of aspiration comprehensively on the basis of bolus viscosity, using clinical, neuroradiological, and videofluoroscopic swallowing study (VFSS) data of patients with pure LMI.

MATERIALS AND METHODS

1. Subjects

Fifty-one subjects with LMI who underwent VFSS between January 2014 and January 2019 at the Department of Rehabilitation Medicine of Yonsei Hospital were enrolled. The inclusion criteria were as follows: (1) patients aged >20 years; (2) patients with pure LMI without any cerebral, cerebellar or pontine involvement confirmed on magnetic resonance imaging (MRI); and (3) patients who underwent VFSS after admission. The exclusion criteria were as follows: (1) patients with a previous history of any neurological disorders such as stroke, traumatic brain injury, brain tumor, Parkinson disease, dementia, and motor neuron disease, and (2) patients with any medical conditions or structural abnormalities of oropharynx that may affect swallowing function.

Sixty-five patients with LMI who underwent VFSS during the study period were screened through a careful medical record review at first. Twelve patients were excluded on the basis of the aforementioned criteria (non-first-ever ischemic stroke). In addition, 2 patients were excluded because of the poor quality of the VFSS image due to difficulty in maintaining posture during the VFSS study. Finally, 51 patents were included in the study.(Fig. 1) This study was approved by the Institutional Review Board of Severance Medical Center.

2. Study design

The medical records, brain magnetic resonance imaging (MRI) scans, and video clips of the videofluoroscopic swallowing studies of the patients were reviewed and analyzed retrospectively. The patients' general characteristics were obtained through their medical charts as follows: age, sex, duration from onset, laterality of lesion and American Speech-Language-Hearing Association National Outcome Measurement System Swallowing Scale (ASHA-NOMS)[14] score. The location of the lesion was assessed using MRI findings (diffusion-weighted axial image) at onset. The functional dysphagia scale (FDS)[15], penetration-aspiration scale (PAS)[16], and temporospatial parameters were assessed using the video clip of the videofluoroscopy of swallowing study. We classified the patients into two groups (aspiration and non-aspiration groups) according to PAS score. The general characteristics, location of the lesion, FDS score, and temporospatial parameters of the VFSS in both groups were analyzed to identify the independ-

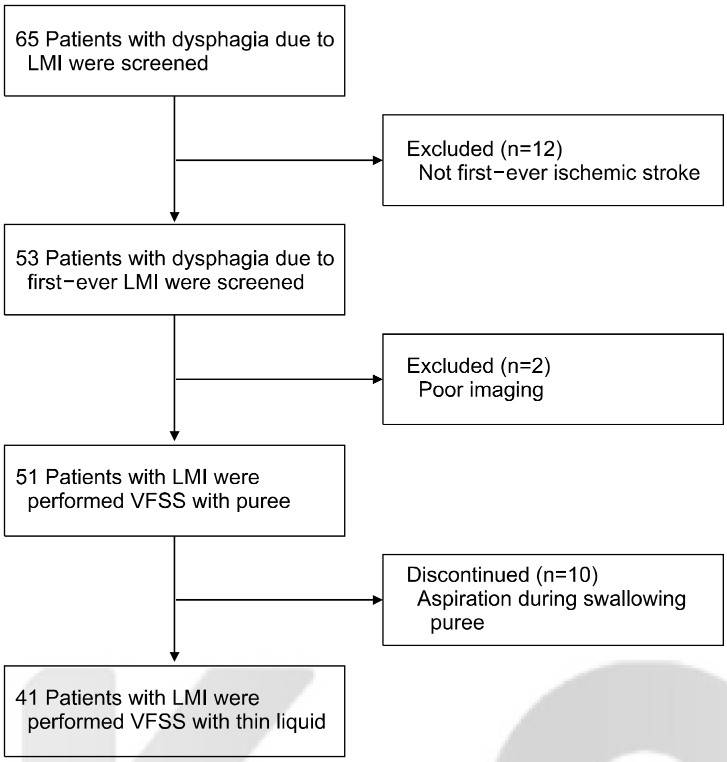

Fig. 1. Patient recruitment flow diagram.

ent significant risk factors of aspiration.

3. Videofluoroscopic swallowing study

The VFSSs were performed at a single center in accordance with the protocol, which consisted of serial administrations and evaluations of swallowing function, with varying volumes of barium viscosities[17]. Each patient received 15 cc of semisolid and thin liquid containing barium consecutively. If aspiration was observed, the test was not continued. The VFSS was performed in the lateral view using radiological fluoroscopy (Winscope, Toshiba, Japan), and images were recorded in real time. Abnormalities in the swallowing process were evaluated in detail using these images. In this study, the liquid used had a viscosity equivalent to level 0 (thin liquid), and the semisolid used had a viscosity equivalent to level 4 (puree) according to the International Dysphagia Diet Standardisation Initiative framework, which was applied to classify the viscosity[18].

To evaluate oral and pharyngeal functions based on the VFSS semi-quantitatively, the FDS was used. It comprises the following 11 items: lip closure score, bolus formation, residue in the oral cavity, oral transit time (OTT), triggering of the pharyngeal swallow, laryngeal elevation and epiglottic closure, nasal penetration, residue in valleculae, residue in pyriform sinuses, coating of the pharyngeal wall after swallow, and pharyngeal transit time (PTT)[15]. The FDS score ranges from 0 to 100, with higher scores associated with more severe dysphagia. For a more quantitative analysis, temporal parameters such as OTT, PTT, and PDT, and kinematic parameters such as laryngeal elevation were measured using the motion imaging analysis software DIPP-Motion V 2D (DITECT Co, Japan).

The PAS was used to identify aspiration, with higher scores associated with more severe aspiration. Aspiration was defined as the passage of material below the level of the vocal cord (PAS score from 6 to 8)[16].

4. Brain MRI

Diffusion-weighted images were acquired using

3.0-T scanners with a standard eight-channel phased array head coil with a single-shot spin-echoplanar imaging sequence. The location of the lesion was classified rostrocaudally and horizontally in accordance with the method used in previous studies[12,13,19-21]. Rostrocaudally, the lesion within the medulla was categorized as follows: rostral medulla, characterized by massive bulging of the dorsolateral area due to the restiform body; middle medulla, characterized by bulging of the lateral surface due to the inferior olive; and caudal medulla, characterized by a relatively round shape without bulging of the lateral surface.

Horizontally, the lesion was also categorized as follows: Diagonal band-shaped lesions sparing the most dorsolateral portion were the most common and therefore designated as the typical type[20,21]. Similarly shaped but more ventrally situated lesions involving some portion of the inferior olive and sparing relatively large portions of the dorsolateral area were classified as the ventral type. Large lesions extending ventrally so as to involve some portion of the olivary nucleus and dorsally so as to involve most (or all) of the dorsolateral area were classified as the large type. Lesions restricted to the most dorsal or dorsolateral portion were classified as the dorsal type. Some lesions, usually at the caudal medulla, were restricted to the lateral, superficial area without extending dorsally and were classified as the lateral type. Other lesions that were not classifiable were designated as the unclassifiable type.(Fig. 2)

5. Statistical analyses

Student t-tests and χ^2 tests were used to compare the aspiration group with the non-aspiration group. Logistic regression analyses were conducted with the forward stepwise method to identify statistically significant risk factors of aspiration. All statistical data were analyzed with SPSS version 18.0 for Windows (SPSS Inc., Chicago, USA). The statistical significance was set at $P<0.05$.

RESULTS

1. Demographic and clinical characteristics

Fifty-one patients (37 men and 14 women) with a mean age of 64.3 years (range, 30-91 years) were evaluated. The lesion was located on the right side in 27 patients and the left side in 24 patients. VFSS was performed 36.2 days (range, 2-228 days) after the onset of stroke.

Subjects were classified according to ASHA-NOMS score as level 1 in 27 patients (52.9%), as level 4 and 5 in 4 patients (7.8%), as level 6 in 9 patients (17.7%) and level 7 in 7 patients (13.7%). The ASHA-NOMS were significantly lower in the aspiration group than in the non-aspiration group during swallowing puree and thin liquid ($P<0.05$, Table 1).

Among the general characteristics, age tended to be older in the aspiration group than in the non-aspiration group in both the puree and thin liquid trials, although the difference was not statistically sig-

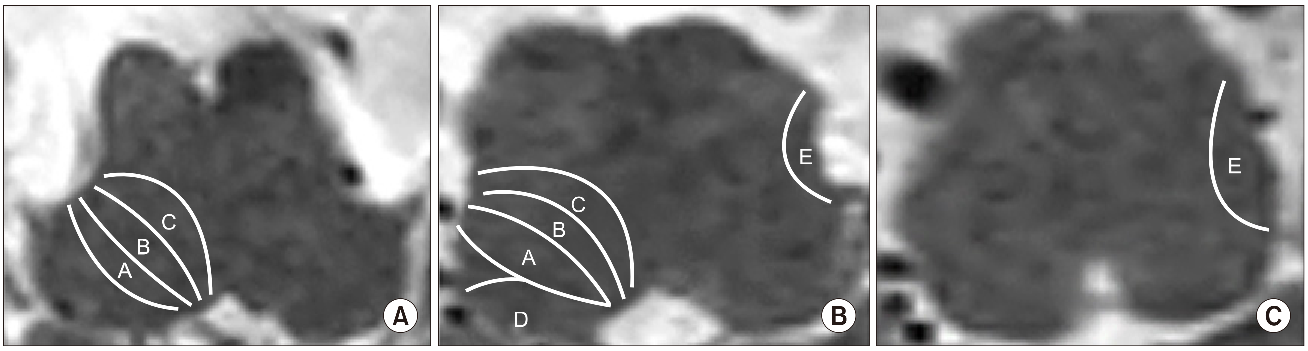

Fig. 2. Definition of lesion location. A+B: typical type, B+C: ventral type, A+B+C: large type, D: dorsal type, E: lateral type. (A) Rostral level. (B) Middle level. (C) Caudal level.

Table 1. Comparison of general characteristics according to aspiration.

Variables	Puree		Thin liquid	
	Aspiration (n=10)	Non-Aspiration (n=41)	Aspiration (n=11)	Non-Aspiration (n=30)
Age (years)	72.10±11.09	62.46±15.97	69.09±14.31	60.03±16.08
Men:Female	7:3	30:11	10:1	21:9
Right:Left side	3:7	24:17	3:8	14:16
Duration (days)	16.90±19.06	40.56±54.88	56.55±70.58	35.13±47.96
ASHA-NOMS	1.30±0.95**	3.73±2.56	2.18±2.09*	4.30±2.51

Values are presented as mean±standard deviations or numbers of cases.
*P<0.05, **P<0.01.
FAC: Functional Ambulation Category, ASHA-NOMS: American Speech-Language-Hearing Association National Outcome Measurement System Swallowing Scale.

nificant (P=0.078 and P=0.108, respectively; Table 1). However, we did not find any significant difference in other factors such as sex, laterality of the lesion, and duration from onset between the groups (P>0.05; Table 1).

2. Location of the lesions

Rostrocaudally, the lesions were located in the rostral medulla (40.0%), middle medulla (45.8%), and caudal medulla (14.3%). Horizontally, most of the lesions were of the typical type (39.2%), followed by the large (31.4%), lateral (7.8%), ventral (5.9%), and dorsal (2.0%) types. The percentage of aspiration was as high as 50.0% in the rostral medulla vertically, and as high as 55.0% and 47.6% in the typical and large type lesions horizontally, respectively.

We found no significant difference in the incidence of aspiration according to the vertical distribution of the lesions (P=0.76, Table 2). However, a significant difference was found in the incidence of aspiration according to the horizontal distribution of lesions and was higher in the group with typical or large lesions (P=0.03, Table 2).

3. VFSS findings

The most common abnormal VFSS findings were residue in valleculae (74.5%), delayed triggering of pharyngeal swallow (72.5%), residue in pyriform sinuses (62.7%), reduced laryngeal elevation (51.0%), coating of the pharyngeal wall after swallow (49.0%),

Table 2. Incidence of aspiration according to lesion location.

	Aspiration	Non-Aspiration	P-value
Vertical			
Rostral	14 (50.0)	14 (50.0)	0.76
Middle	13 (40.6)	19 (59.4)	
Caudal	4 (40.0)	6 (60.0)	
Horizontal			
Typical/Large	20 (48.8)	21 (51.2)	0.03*
Others	1 (10.0)	9 (90.0)	

Values are presented as numbers of cases (%).
*P<0.05.

and delayed PTT (56.9%; Fig. 3).

Aspiration was detected in 21 (41.2%) of the 51 patients who received puree or thin liquid. Aspiration occurred in 10 (19.6%) patients who received puree and 11 (26.8%) patients who received thin liquid.

The total scores of FDS were significantly higher in the aspiration group than in the non-aspiration group during swallowing puree and thin liquid (P<0.05). The FDS subscores for residue in valleculae, residue in pyriform sinuses, and PTT measured in kinematic analyses were significantly higher in the aspiration group than in the non-aspiration group during swallowing of puree (P<0.05). In addition, the FDS subscores for residue in valleculae, residue in pyriform sinuses, coating of the pharyngeal wall, and PDT measured in kinematic analyses were significantly higher in the aspiration group than in the non-aspiration group while swallowing thin liquid (P<0.05; Table 3).

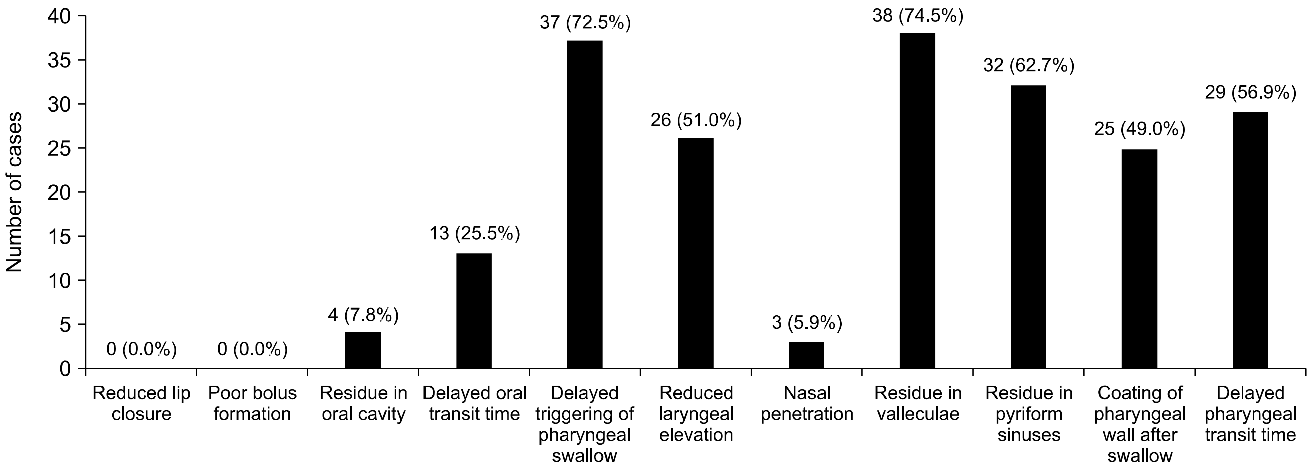

Fig. 3. Incidence of abnormal swallowing functional process using functional dysphagia scale (FDS).

Table 3. Comparison of general characteristics according to aspiration.

Factors	Puree		Thin liquid	
	Aspiration n=10	Non-Aspiration n=41	Aspiration n=11	Non-Aspiration n=30
Lip closure	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
Bolus formation	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
Residue in oral cavity	0.20±0.63	0.15±0.53	0.00±0.00	0.00±0.00
OTT[1)] (sec)	1.22±1.27	0.88±1.39	0.28±0.21	0.22±0.10
PDT[1)] (sec)	1.01±2.26	0.85±2.15	0.18±0.33*	0.02±0.14
Laryngeal elevation[1)] (mm)	22.93±3.64	22.74±5.58	22.34±5.44	23.02±5.58
Nasal penetration	0.80±1.69	0.00±0.00	0.36±1.21	0.00±0.00
Residue in valleculae	7.60±2.95*	4.39±3.77	5.82±2.09**	2.40±2.90
Residue in pyriform sinuses	10.40±2.07**	3.61±4.27	5.45±2.02**	2.27±3.59
Coating of pharyngeal wall after swallow	5.00±5.27	4.88±5.06	8.18±4.05**	2.67±4.50
PTT[1)] (sec)	16.06±23.18**	2.41±5.43	1.65±2.32	0.79±0.62
Total FDS	38.60±10.29*	25.90±14.97	32.36±11.59**	17.20±14.20

Values are presented as mean±standard deviations.
[1)]Values was measured by kinematic analyses.
*$P<0.05$, **$P<0.01$.
OTT: Oral Transit Time, PDT: Pharyngeal Delayed Time, PTT: Pharyngeal Transit Time.

4. Risk factors of aspiration

In the logistic regression analyses, the significant risk factors of aspiration were residue in pyriform sinuses during swallowing of puree, and prolonged PDT and residue in valleculae during swallowing of thin liquid ($P<0.05$; Table 4).

DISCUSSION

We investigated the characteristics of dysphagia and the risk factors of aspiration in patients with pure LMI comprehensively, with an analysis of VFSS study results. In this study, we revealed that the location of the lesions and a disturbed swallowing pattern in the pharyngeal phase may affect the aspiration of bolus. To our knowledge, this is the first study to identify the risk factors of aspiration on the basis of VFSS

Table 4. Logistic regression of risk factors for aspiration.

Variable	Odd ratio	95% CI	P-value
Puree			
PTT			0.07
Residue in valleculae			0.72
Residue in pyriform sinuses	1.53	1.17-2.01	0.00*
Horizontal distribution (Large, Typical type)			0.26
Thin liquid			
PDT	285.61	2.24-36415.28	0.02*
Residue in valleculae	1.86	1.20-2.88	0.01*
Residue in pyriform sinuses			0.61
Coating of pharyngeal wall after swallow			0.17
Horizontal distribution (Large, Typical type)			0.94

*$P<0.05$.
PTT: Pharyngeal Transit Time, PDT: Pharyngeal Delay Time.

results in patients with LMI.

Old age tended to be associated with a high incidence of aspiration in this study, although the association was not statistically significant. However, sex, laterality of the lesion, and duration from onset were not related to aspiration. The effect of old age on aspiration in patients with LMI is still unclear. Most previous studies showed that oropharyngeal dysphagia was a highly prevalent and increasing condition in the older population and in patients with pneumonia[22,23]. The increased prevalence of dysphagia in the elderly increased the risk of pneumonia[24]. However, Oshima et al.[7] reported that age was not significantly associated with severity of dysphagia in patients with LMI, and Cho et al.[25] reported that no significant difference in age was found between the severe and non-severe dysphagia groups of patients with LMI. We think that bolus aspiration may increase with age-related physiological changes, but comorbidities and severity after stroke may have more influence on bolus aspiration. Aging itself was not an isolated risk factor as Jardine et al.[26] suggested.

Topographically, aspiration was more frequent in the patients with typical or large type lesions, and we did not find a significant location related to aspiration vertically in this study. Several studies reported controversial results regarding the location of anatomical lesions being related to the severity of dysphagia. Kim et al.[12] reported that rostral lesions of the medulla were associated with more severe dysphagia, while Ogawa et al.[27] reported that dysphagia occurred in patients with lesions in the rostral or middle part of the medulla. Oshima et al.[7] reported that the horizontal extent of the lesion was not found to be strongly related to the severity of dysphagia. Cho et al.[25] reported that the severe group showed posterolateral involvement in the rostral or caudal area of the medulla.

Swallowing mainly depends on the CPG located in the medulla oblongata in the ventrolateral medulla[28]. However, aspiration may occur by not only invasion of the CPG but also invasion of the premotor neurons that interconnect bilateral CPGs in the medulla[5]. CPGs on both sides are interconnected extensively[5] and premotor neurons that can affect the swallowing function might be located at the posterolateral part and spread vertically as Cho et al.[25] suggested.

In this study, the abnormal findings during swallowing in LMI, such as residue in valleculae, delayed triggering of pharyngeal swallow, residue in pyriform sinuses, delayed PTT, reduced laryngeal elevation, and coating of the pharyngeal wall after swallow, were found mainly in the pharyngeal phase and seldom in the oral phase. This may mean that the dysphagia in patients with LMI mainly resulted from pharyngeal dysfunction, unlike other post-stroke lesions that resulted from oral dysfunction, despite the fact that post-stroke patients generally show dysfunction in the oral and pharyngeal phases[29-31]. The findings in this study were consistent with those of previous studies that reported delayed and slow swallowing reflex, reduced pharyngeal contractions, UES opening failure, and disruption of the spatiotemporal pattern in LMI[5-11]. This may be explained by the disrupted function of the swallowing center after LMI, which coordinates the pharyngeal and esophageal phases of swallowing[6]. The swallowing center consists of the nucleus tractus solitaries (NTS), nucleus ambiguous (NA), and reticular formation located in the dorsolateral medulla[5].

This study showed that residue in valleculae, residue in pyriform sinuses, and prolonged PTT were significantly associated with aspiration of food bolus. These results were similar to those of previous studies that reported that residue in valleculae and pyriform sinuses were associated with the highest comorbidity rate with aspiration and had poorer treatment outcomes[32,33]. Moreover, prolonged PDT was significantly associated with aspiration when swallowing thin liquid. This result is consistent with that of a previous report showing that not only prolonged PTT but also prolonged PDT is an important temporal determinant of aspiration in stroke patients[34]. By contrast, another study showed no significant differences in the temporal parameters between the aspirators and non-aspirators during swallowing of liquid in the patients with dysphagia[35].

This study showed that residue in pyriform sinuses was a significant independent risk factor of aspiration in swallowing puree and that prolonged PDT and residue in valleculae were significant independent risk factors of aspiration in swallowing liquid among all the examined clinical factors, lesion locations, and swallowing processes. It is in line with the report of Oshima et al.[7] in that the presence of a passage pattern abnormality can be a useful predictor of severe dysphagia in LMI. Residue in pyriform sinuses may be caused by cricopharyngeal dysfunction (CPD), defined as narrowing at the level of the UES caused by absent or incomplete sphincter opening[8]. The cricopharyngeal muscles are controlled by the medulla; thus, medullary infarction may result in failed relaxation of the UES[5]. As the bolus could not pass through the UES, it finally overflows to the glottis from the pyriform sinus[36]. Prolonged PDT and delayed elevation of the larynx may be caused by the disruption of the swallowing center located in the lateral medulla. The sensory fibers that activate the reflexive pharyngeal swallow from the pharyngeal branch of the glossopharyngeal nerve (CN IX) and superior laryngeal nerve of the vagus (CN X) travel to the medulla, where they synapse in the NTS. Thus, as in this study, prolongation of the PDT in LMI patients with NTS lesions may be a natural consequence. Therefore, the prolonged PDT could lead to increased duration of the larynx opening and result in aspiration.

It is interesting how the risk factors of aspiration differed depending on bolus viscosity in this study. The damage to the swallowing center in LMI resulted in decreased coordination of the swallowing muscles and delayed muscle activity. Increasing bolus viscosity has been well known to result in increased safety of swallowing[37,38]. Despite that the temporo-kinematic changes in bolus viscosity were still unclear, these findings of the present study could be explained by the previous studies. Newman et al.[37] suggested that a bolus with high viscosity resulted in increased amounts of oral and/or pharyngeal residue, which may result in aspiration. Sia et al.[39] reported that the pharyngeal swallowing power was higher in the pudding bolus than in the thin liquid bolus[39]. Dantas et al.[40] revealed that the mean flow rate through the UES for liquid viscosity was significantly faster than that for paste viscosity in a VFS manometric study of healthy volunteers. Wu et al.[41] suggested that it increased the sensory afferent stimulation to the pharyngeal cavity, thereby effectively reducing the incidence of aspiration. Therefore, as shown in our results, CPD can be the major aspiration risk factor in swallowing puree but not in swallowing thin liquid.

This study has some limitations. The retrospective design of this study may have increased the possibility of bias with respect to the review of the demographic, radiological, and clinical data of the patient series. The duration from onset was variable despite that only patients who underwent a VFSS study first after onset were enrolled. The statistical bias could not be excluded because the distribution of involvement was unequal. The patients with typical or large type lesions was more enrolled than that in other type lesions. Only patients who were referred for VFSS study were enrolled; thus, the results cannot be generalized. Finally, only a small number of patients were enrolled in this study, although the study population was larger than those of previous related studies. Therefore, further large-scale, prospective, multicenter studies are needed to confirm our study results.

CONCLUSION

This study shows that residue in pyriform sinuses may be an independent risk factor of aspiration in swallowing puree, while prolonged PDT and residue in valleculae may be independent risk factors of aspiration in swallowing liquid among all clinical factors, lesion locations, and swallowing processes. These findings of this study may be helpful in understanding aspiration and in planning a more appropriate treatment program for patients with LMI.

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